REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1-10 were pending in this application when last examined.

Claims 3 and 4 were examined and stand rejected.

Claims 1, 2 and 5-10 were withdrawn as non-elected subject matter.

Claims 3 and 4 are amended to recite "isolated and optically active". Support for such is inherent throughout the specification, for example on page 3, lines 22-23, page 9, lines 22-40, and page 14, line 16.

No new matter has been added.

Applicants further note that Claim 3 and 4 were previously amended in the reply filed March 6, 2007 to recite the term "optionally". During the personal interview, the Examiner and her supervisor noted that such an amendment may not be supported. Applicants note that such term is inherently supported by the original claim language. In particular, the original claims called for administering the compound itself **or** a composition containing the compound and a carrier. Thus, claims 3 and 4 have merely been simplified by stating that the compound and "optionally" a carrier is administered. Applicants therefore suggest these claim amendments are supported by the claims as filed.

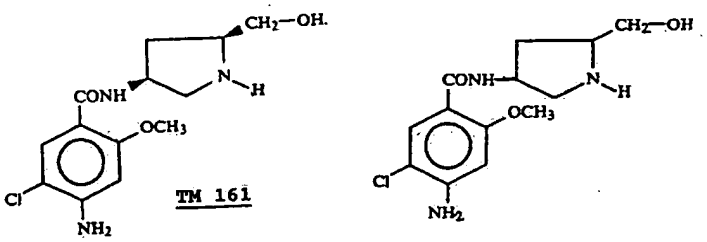
II. ANTICIPATION/OBVIOUSNESS REJECTION

On page 2 of the previous Office Action, claims 3 and 4 were again rejected under 35 U.S.C. § 102 as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over U.S. Patent 5,143,935.

Applicants respectfully traverse this rejection, as applied to the amended claims, for reasons of record and for the following reasons.

The cited U.S. Patent 5,143,935 describes administration of racemic modification (racemate), 4-amino-5-chloro-2-methoxy-N-[2-hydroxymethyl-4-pyrrolidinyl]benzamide. As you see, its (2S, 4S) stereoisomer is TM161 of the present invention. The racemic modification,

4-amino-5-chloro-2-methoxy-N-[2-hydroxymethyl-4-pyrrolidinyl]benzamide in Example 10 of U.S. Patent 5,143,935 vaguely contains (2S, 4S) stereoisomer, i.e. TM161 of the present invention.



However, the cited reference does not disclose the administration of isolated and optically active TM161 or a composition containing it. In other words, the cited reference does not disclose the administration of the composition containing isolated and optically active TM161 with substantially no other stereoisomers.

Furthermore, as noted in our last reply, the cited reference does not provide enabling disclosure for production of the claimed isomer. In particular, the cited reference discloses a method for production of the racemate. On the other hand, as noted in the previous response, the inventors found it necessary to create a new synthetic method to obtain the claimed stereoisomer. Furthermore, also as noted previously, the claimed stereoisomer cannot be isolated by conventional crystallization and may only possibly be isolated by chromatography through intensive and undue trial and error. Also, there was no teaching or suggestion at the time of filing of the present application on how to isolate the claimed stereoisomer. Thus, the cited reference fails to teach or suggest this stereoisomer of the amended claims because it fails to provide an enabling disclosure for producing only the claimed stereoisomer. Please see MPEP 2121.02 and Force Laboratories, Inc. v. IVAX Pharmaceuticals, Inc., 501 F.3d 1263, (C.A. Fed. (Del.) September 5, 2007).

Also, as noted in our previous response, the claimed invention exhibits unexpected effects not taught by the prior art reference. In this regard, Applicants note there was an error in the Supplemental Response filed December 31, 2007. In particular, page 4, lines 1 and 2, should have read "these results indicate that the binding affinity of TM161 is 8.9 times ~~greater~~ weaker than that of TKS159." Applicants made this error without any deceptive intent.

Furthermore, in the 132 Declaration submitted December 31, 2007, Applicants set forth results of side-effect and safety testing of a claimed compound as compared to the cited compound. The Examiner is respectfully requested to enter this Declaration.

The submitted data showed that the claimed compound unexpectedly does not cause thrombus formation, arteritis or encephalomalacia. Shown below is the data presented in the Declaration.

A. Side-effects

The binding affinity for TM161 and TKS159 for the dopamine D2 receptor

Test drugs	IC_{50} μM
TM161	34
TKS159	3.8

These results indicate that the binding affinity of TM161 is 8.9 times weaker than that of TKS159. Binding with dopamine D2 receptor is a cause of side-effects, such as extrapyramidal sign.

B. Safety

TM161 was administered orally to three beagle dogs at a dose of 100 mg/kg once a day for 4 weeks.

Pathohistological tests were performed using a light microscope and abnormalities were not found. Further, neither thrombus formation, arteritis nor encephalomalacia was identified.

On the other hand, TKS159 was administered orally to three beagle dogs at a dose of 30 mg/kg once a day for 4 weeks.

Pathohistological tests were performed using a light microscope and abnormalities were not found. Further, neither thrombus formation, arteritis nor encephalomalacia was identified.

Applicants therefore note that TM161 can be administered in a 3.3 times larger dose than TKS159 without engendering side effects.

Thus, the anticipation/obviousness rejection over the '935 patent is untenable because (1) the cited reference fails to disclose administration of isolated and optically active TM161 or a composition containing it, (2) the cited reference is non-enabling for production of the claimed stereoisomer, and (3) the cited reference does not render obvious the claimed invention because such reference fails to teach the unexpected results of the claimed invention. For these reasons, Applicants suggest that this rejection is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested. If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

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